

Remarks

Under Examination are claims 19, 20 and 29, drawn to a polypeptide of SEQ ID NO: 16. All other claims have been previously canceled or canceled herein.

Claim 19 has been amended herein by amending the phrase "one or more conservative amino acid substitutions" to instead recite "one to twenty conservative amino acid substitutions". This amendment is supported throughout the specification as filed, particularly at page 7, lines 25-32, page 5 lines 8-19, and in the claims.

Response to 35 U.S.C. § 112 Rejection, First Paragraph, Written Description

Claim 19 stands rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking adequate written description.

The Examiner asserts that the claim is drawn to a genus, i.e., single or multiple substituted sequences of SEQ ID NO:16 or single mutations of SEQ ID NO:16 represented by a single amino acid deletion, insertion or substitution. The Examiner cites *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997) to support the rejection.

The Examiner further asserts that there is a lack of representative examples that would demonstrate possession of the genus at the time of filing. It is the view of the Examiner that there are a minimum of 124 possible amino acid deletions or insertions to be had on the amino acid sequence that have not been discussed or described. The Examiner further asserts that up to 124 substitutions can be made at a single time, inferring that not one amino acid would remain from the original sequence of SEQ ID NO:16.

Although not necessarily agreeing with the reasoning of the Examiner, Applicants have amended claim 19 in order to expedite prosecution of the application. Applicants respectfully submit that claim 19 as amended is amply described in the specification as filed and request that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn for the following reasons.

In *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991), the Court of Appeals for the Federal Circuit traced the development of the written description requirement under 35 U.S.C. § 112, first paragraph. The *Vas-Cath* Court, in a unanimous opinion, noted approvingly that in a written description analysis, "[t]he primary concern is factual and depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure." *Vas-Cath*, 19 USPQ2d at 1116 (quoting *In re Wertheim*, 191

USPQ 90, 96 (C.C.P.A. 1976)). After discussing the policy reasons underlying the requirement, the Court set forth the standard for the written description requirement:

The purpose of the “written description” requirement is broader than to merely explain how to “make and use”; the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. . . . The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon “reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter.”

Vas-Cath, 19 USPQ2d at 1117 (emphasis added) (quoting *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 227 USPQ 177, 179 (Fed. Cir. 1985)). *Accord Regents of University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), cited by the Examiner. Therefore, it is well-settled that the knowledge of those skilled in the art informs the written description inquiry.

In *In re Alton*, 37 USPQ2d 1578, 1584 (Fed. Cir. 1996), the Court of Appeals for the Federal Circuit pointed out that literal support is not required in order to satisfy the written description requirement:

If a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met. For example, in *Ralston Purina Co. v. Far-Mor-Co., Inc.*, 227 USPQ 177, 180 (Fed. Cir. 1985), the trial court admitted expert testimony about known industry standards regarding temperature and pressure in “the art of both farinaceous and proteinaceous vegetable materials.” The effect of the testimony was to expand the breadth of the actual written description since it was apparent that the inventor possessed such knowledge of industry standards of temperature and pressure at the time the original application was filed.

It is clear that the invention need not be described in *ipsis verbis*, *i.e.*, literally, for purposes of the written description requirement under 35 U.S.C. §112, first paragraph, whether or not a genus or species is being described and claimed. Rather, what is needed is that the skilled artisan understand, based upon the disclosure in the specification as filed, and the knowledge imputed to the skilled artisan at the time the specification was filed, that the inventor had possession of the claimed subject matter.

Even more recently, the PTO Board of Patent Appeals and Interferences and the Federal Circuit have addressed the role of sequences and the written description requirement. In *Capon v. Eshhar* (Fed. Cir., No. 03-1480 (8/12/05); 2005 U.S. App. LEXIS 16865; copy provided herewith) the court examined a need for supplying sequences, when the base sequence is known in the art. The court stated on the last page that “[i]n summary, the Board erred in ruling that § 112 imposes a per se rule requiring recitation in the specification of the nucleotide sequence of claimed DNA, when that sequence is already known in the field. However, the Board did not explore the support for each of the claims of both parties, in view of the specific examples and general teachings in the specifications and the known science, with application of precedent guiding review of the scope of claims”. Thus, the *Capon* court held that if a sequence is known, then that sequence need not be recited again if it is known in the field, because there is no per se rule to do so. In other words, a residue by residue analysis is not required when the structure of the component nucleic acid or protein segments are already known, or are readily determined by known procedures.

In the present case, by disclosing the base sequence herein, there is no need to supply the modified sequences which would only comprise up to 20 conservative amino acid residue changes of a 124 amino acid sequence as claimed in amended claim 19, because one of ordinary skill in the art would understand what is claimed and how to prepare the claimed modifications.

Additionally, in *Ex parte Olga Bandman* (BPAI Appeal No. 2004-2319; Application No. 09/915,694; submitted herewith), the Board of Patent Appeals and Interferences addressed the written description requirements for species and genus relations. As the BPAI stated at page 3, the written description requirement does not require a description of the structure of every species (citing *Utter v. Hiraga*, 845 F.2d 993, 998, 6 USPQ2 1709, 1714 (Fed. Cir. 1988) (“A specification may, within the meaning of 35 U.S.C. § 112, ¶ 1, contain a written description of a broadly claimed invention without describing all species the claim encompasses.”). The BPAI in *Bandman* goes on to say that “[w]hile the examiner asserts that the specification provides no disclosure of any particular structure to function/activity relationship in the single disclosed species, the examiner has not adequately explained and/or provided evidence to support that assertion” (*Ex parte, Bandman*, page 5).

As described above, claim 19 has been amended herein by amending the phrase “one or more conservative amino acid substitutions” to instead recite “one to twenty conservative

amino acid substitutions”. That is, the claim as amended recites only a limited number of modifications or conservative amino acid substitutions, now limited to twenty or fewer, of SEQ ID NO:16. One of ordinary skill in the art would understand how to prepare a peptide comprising one to twenty conservative amino acid substitutions based on the specification as filed. Furthermore, as amended, the modifications do not encompass a genus of peptides which could potentially contain none of the original amino acid residues. Further, one of ordinary skill in the art would appreciate that such sequences are adequately described in the specification as filed. This amendment is supported throughout the specification as filed, particularly at page 7, lines 25-32, page 5 lines 8-19, and in the claims. For example, at page 7, the substitution of twenty or fewer amino acids is described. Additionally, at page 5, a list is provided which describes specifically which amino acids are known to be amenable to conservative substitution and lists the amino acids which are interchangeable with one another.

Applicants respectfully submit that the skilled artisan would have understood, based upon the disclosure provided in the specification as filed, that the inventors had possession of the present invention as claimed.

Response to 35 U.S.C. § 102(e) Rejection

The Examiner has rejected claims 19, 20, and 29 as allegedly anticipated by U.S. 2002/0102604 (Edwards et al.) under 35 U.S.C. § 102(e). The Examiner asserts that SEQ ID NO:266 of Edwards is the sequence of the instantly claimed SEQ ID NO:16 and that it is antigenic.

Applicants traverse the rejection for the following reasons.

Submitted herewith under 37 C.F.R. § 1.131 is a Declaration by Dr. John Herr, an inventor of the present invention, asserting that the presently claimed invention was invented before Edwards et al. was filed, asserts and verifies that the Edwards application, which claims the benefit of provisional application filed December 8, 1999, was not filed before the instant invention for patent by the Applicants and therefore cannot anticipate the presently claimed invention under 35 U.S.C. § 102(e).

The documentation provided with the Declaration comprises 68 photocopied pages of the laboratory notebook of one of the co-inventors, Dr. Jagathpala Shetty, who performed much of the work of the present application. The 68 pages were all dated at the time of data entry and are labeled as Exhibits 1 through 68. All of the laboratory notebook pages also

indicate the name of the person entering the data, namely Jagathpala Shetty. The pages are dated from August 12, 1999 to December 18, 1999. The invention disclosure was then prepared by the Applicants and submitted to the University of Virginia Patent Foundation. A provisional patent application was then prepared and filed on January 19, 2000. Therefore, the entire process of identifying the protein called C58, isolating it, sequencing it, performing bioinformatic analyses, protein expression and northern blot analyses, was performed from August 12, to December 18, 1999. The data were then compiled, an Invention Disclosure was prepared and submitted to the University of Virginia Patent Foundation, and a patent application was prepared and filed within a month of the last dated laboratory notebook page.

Examiner is reminded that the present application is a Divisional application and that two other proteins were prosecuted in the parent application (now issued) encompassing the peptide of SEQ ID NO:2 and the nucleic acid sequence encoding SEQ ID NO:2, and another active Divisional application encompassing SEQ ID NO:9. All of the work encompassing the various proteins was occurring simultaneously and was included in the provisional application.

The progress of the experiments related to identifying the sequence of the peptide named C58, which has the sequence of SEQ ID NO:16, will be summarized below to demonstrate when the sequence was first discovered and to demonstrate diligence in completing the invention. However, it should be noted that the complete nucleotide and amino acid (SEQ ID NO:16) sequences of C58 were first demonstrated in the laboratory notebook of Dr. Shetty on October 5 and 6, 1999 on pages 82-84 (Exhibits 35-37).

The first page of evidence supplied with the Declaration (Exhibit 1; page 39 of the notebook, dated August 12, 1999) has a copy of an image of a two-dimensional gel which is labeled with numbers to identify locations of various proteins which were partially sequenced on August 11, 1999, including C58 (the name of the protein comprising SEQ ID NO:16). The spots had been cored from the gel, subjected to tryptic digests, and subjected to microsequencing, the results of which are indicated in Exhibit 2, dated August 15, 1999. Exhibit 2 demonstrates the four peptide tryptic digest components of spot/band C58.

Exhibit 3 (page 42 of the notebook, dated August 15, 1999) depicts the use of an EST chosen based on the tryptic digests.

Exhibits 4 to 34 (comprising laboratory notebook pages 43, 48, 50-54, 56-75, and 77-80, respectively; dated August 26 to September 25, 1999), demonstrate a series of experiments and data involving further preparation and isolation of the C58 nucleic acid and

peptide sequences. Exhibit 4 demonstrates the PCR strategy using the EST and Exhibit 5 demonstrates the sequence of the PCR-derived EST partial sequence for C58. Exhibit 6 (page 50, dated September 7, 1999) summarizes the cloning of C58 and the beginning of several weeks work of screening the C58 library (Exhibits 6 to 79; dated September 7, 1999 to September 30, 1999).

A nucleic acid sequence was obtained and disclosed in Exhibit 35 (page 82 of the notebook, dated **October 5, 1999**). The sequence for the nucleic acid encoding the amino acid sequence of SEQ ID NO:16 (C58 protein) included the ORF of the sequence. The sequence was examined and Exhibit 37 (page 84 of the notebook, dated **October 6, 1999**) presents the deduced 124 amino acid residue sequence of SEQ ID NO:16.

Therefore, it can be seen that the nucleic acid sequence encoding SEQ ID NO:16 was obtained by **October 5, 1999**, and at that point the nucleic acid sequence was capable of being used to deduce the amino acid sequence, which amino acid sequence (i.e., SEQ ID NO:16) was indeed demonstrated on Exhibit 37, dated **October, 6, 1999**. These two dates indicating the C58 sequences are much **earlier** than the December 8, 1999 filing date of the Edwards provisional application.

Next, a series of bioinformatic analyses were performed to compare the new sequences to other sequences known in the art and to further characterize the protein. Then, a series of experiments and analyses were performed to ensure that the complete protein had been isolated and sequenced, expression vectors were prepared and analyzed, and cells were transformed with the expression vectors and analyzed (see Exhibits 38-52, performed until November 23, 1999). For example, Exhibit 52 (the carbon copy page of page 100, with a sequence pasted in; dated November 23, 1999), demonstrates the sequence alignment of C58 with proteins of the Ly6/UPAR family of proteins.

Exhibit 53 is a copy of page from a new notebook (page 1, dated November 29, 1999) where a series of experiments analyzing protein expression from the bacterial vector were begun. These experiments are illustrated in Exhibit 53 to Exhibit 63 (comprising notebook pages 1-6, and 9-13, respectively; dated November 29, 1999 to December 15, 1999).

Next, a series of experiments were performed to verify that the newly discovered C58 protein, which was discovered in testis, was indeed a testis specific protein. To that end, a series of probes and reagents were prepared and Northern blot analyses were performed, finding testis specific expression of C58 (see Exhibits 64 to 68, comprising notebook pages 14-18, respectively, dated December 15 to December 18, 1999).

The C58 experiments performed to that date (December 18, 1999) were then included as part of an invention disclosure, along with the results of two other proteins. The invention disclosure was submitted to the University of Virginia Patent Foundation, reviewed, and prepared and filed as a provisional patent application on January 19, 1999. Thus, it can be seen that from the time of the last C58 experiment included in the application, the time required to prepare and submit the invention disclosure and prepare and file a provisional patent application was only one month. These acts all indicate diligence in inventing, reducing to practice, and filing an application based on the three proteins which were included in the original provisional application.

Based on the description provided above, the 37 C.F.R. § 1.131 Declaration provided by inventor Dr. John Herr indicating the veracity of the statements above, the evidence provided with the Declaration in the form of dated copies of the laboratory notebook of inventor Dr. Jagathpala Shetty, who worked in Dr. Herr's lab, Applicants assert that the present invention was clearly not anticipated by Edwards et al. under 35 U.S.C. § 102(e). Therefore, Applicants respectfully request that the anticipation rejection as to amended claim 19 be withdrawn.

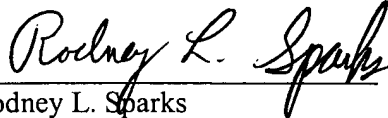
Applicants respectfully submit that based on the arguments presented above, amended claim 19, and claims 20 and 29, are in condition for allowance.

Conclusion

If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (434) 243-6103.

Respectfully submitted,

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